AMENDMENTS TO THE DRAWINGS:

After FIGURE 6, please insert FIGURE 7. (Attachment 1)

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REMARKS

Applicant is grateful to the Examiner for allowing claim 88 of the instant application. However, reconsideration of the other claims in above-identified application is respectively requested in view of the above amendments and the following remarks. The Examiner objected to claims 1, 24, and 85 and rejected claims 1, 10, 14, 24, 25, 86, 87, and 89 for multiple reasons. Claims 1 and 24 have been amended. Claims 85 and 88 are hereby withdrawn from consideration without prejudice. Claims 90-98 have been added. Claims 1, 10, 14, 24, 25, and 86, 87, and 89-98 are currently under consideration. The support for the amendment to claim 1 is in claim 88. The support for the newly added claim 90 is derived from the specification and the explanation of Dr. Kaemmerer during the interview with the Examiner, as described in details below. The support for the newly added claims 91-98 is found in claims 10, 14, 24, 25, and 86, 87, and 89 and page 29 of the specification. Pages 9, 14, 29-35 of the specification have also been amended to incorporate material from a U.S. Application SN 09/872,698 and also correct minor spelling errors. Accordingly, this Amendment adds no new matter to the application as filed on November 25, 2003.

Applicant's invention is directed to *inter alia* a medical system for treating a spinocerebellar ataxia type 1 in a human live patient comprising: (a) an intracranial access device; (b) a mapping means for locating a predetermined intraparenchymal location in the brain of the patient, said location comprising neurons natively expressing a gene encoding an ataxin-1 protein; (c) a deliverable amount of a small interfering RNA capable of reducing the amount of ataxin-1 protein produced in said neurons, or a vector encoding said small interfering RNA, wherein said small interfering RNA has a length of between about 15 and about 30 nucleotides and comprises any one of SEQ ID Nos: 1 and 2; and (d) a delivery means for delivering said small interfering RNA or vector encoding said small interfering RNA to said location of the brain of said patient from said intracranial access device through a stereotactically implanted catheter.

In another aspect, the invention provides a medical system for treating spinocerebellar ataxia type 1 in a human patient comprising: (a) an intracranial access device; (b) a patient-specific mapping means for allowing stereotactical implantation of the device in a predetermined location in the brain of the patient, said location comprising

cells natively expressing a gene encoding an ataxin-1 protein; (c) a deliverable amount of a small interfering RNA capable of reducing the amount of ataxin-1 protein produced in said cells or a vector encoding said small interfering RNA; and (d) a delivery means for delivering said small interfering RNA or vector encoding said small interfering RNA to said location of the brain of said patient from said intracranial access device through a stereotactically implanted catheter.

AMENDMENTS TO THE SPECIFICATION AND CLAIMS

Pursuant to 37 CFR § 1.57, incorporated information from another U.S. patent application is as much a part of the application as filed as if the text was repeated in the application and should be treated as part of the text of the application as filed. Replacing the identified material incorporated by reference with the actual text is not new matter. (see MPEP § 2163.07(b)).

Applicant also makes the statement that "the material being inserted into the specification is the material that previously incorporated by reference from US Application SN 09/872,698 at page 29 of the instant specification and that the amendment contains no new matter."

The support for the newly added claims 90 and 98 and the limitations articulated in the step (b) of said claims is derived from the Application SN 09/872,698; filed on June 01, 2001, issued as US Patent 7,189,222 ("the '698 Application" see Attachment 2) on March 13, 2007, as originally incorporated by reference in the instant specification. (see instant Specification at page 29, line 18). Figure 7 of the '698 Application has been incorporated in the instant application in compliance with 37 CFR §§ 1.121 and 1.184. The support for the newly added limitations is found at Figure 7; page 5, lines 29-30; page 11, lines 9-15, 22-29, and page 12, lines 1-10 of the '698 Application. Accordingly, this Amendment adds no new matter to the instant application as filed on November 25, 2003.

Claim 98 is added to address Examiner's concerns and Applicant's position as articulated during the interview. In doing so, Applicant has merely made explicit what has been implicit and inherent in the original application by incorporating the language directly from the '698 Application. Accordingly, Applicant believes that the presented claims are clearly distinguished from McCaffrey et al.

In essence, the instant invention rather than relying on pre- or post- surgical mapping or imaging techniques of a patient's brain, employs such imaging procedures as guided stereotactical and triangulation techniques *during the actual brain surgery* to enhance delivery of siRNA to the locations of interest.

CLAIM OBJECTIONS

The Examiner objected to claim 1 asserting that the terms "live" and "patient" are redundant and the term "patient" inherently designates a living system, e.g., a human. Applicant amended claim 1 to remove the term "live" from the claim.

The Examiner also objected to claim 24 because of indication of the relationship between the "port" with any other elements of the system. Claim 24 in its amended form specifies that the intracranial access port is a part of the intracranial access device specified in claim 1.

The Examiner further objected to claim 85 as being an improper dependent claim failing to further limit the scope of the claim it depends from. Applicant withdraws claim 85 without prejudice.

The Applicant thanks the Examiner for bringing these comments to the Applicant's attention and respectfully requests that the objections be withdrawn in view of the previous remarks.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner rejected claims 1, 10, 14, 24, 25, and 85-89 for indefiniteness. Before the instant amendment, claim 1 recited "small inhibitory RNA" without insufficient antecedent basis. The other pending claims were rejected due to their dependence on claim 1. The Examiner correctly pointed out that the recitation appears to be a typographical error. Applicant is grateful to the Examiner for noticing this error. In the newly amended form, claim 1 does not recite "small inhibitory RNA". Accordingly, Applicant respectfully requests that this ground for rejection be removed.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner rejected claims 1, 10, 14, 24, 25, and 85-89 under 35 USC § 112, first paragraph asserting that the requirement that the small interfering RNA should target a portion of SCA-1 mRNA which is at least 9 bp downstream of the transcription start

site. Applicant respectfully notes that the specification discloses siRNA sequences which bind a portion of SCA-1 located mRNA more than 9 bp downstream of the transcription start site (e.g., 945-965). Nevertheless, in the interest of the expedited prosecution, the Applicant removed this limitation from claim 1. Accordingly, Applicant respectfully requests the Examiner to withdraw this ground for rejection.

PROVISIONAL OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION (PREVIOUS)

The Examiner further rejected claims 1, 10, 14, and 25 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 7, 8, 16, 17, and 29 of a co-pending application No. 10/962,732.

MPEP § 804(I)(B)(1) recites as follows:

> [i]f a 'provisional' nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicant respectfully notes that the instant application was filed on November 25, 2003. while application No. 10/962,732 was filed later, on October 12, 2004. Therefore, the instant application is the earlier-filed application of the two applications. Applicant further notes that as of May 21, 2007, no action on merits have been taken regarding the later-filed application No. 10/962,732.

Accordingly, without making any admissions or agreeing with the Examiner, Applicant respectfully requests postponement of any action on this ground of rejection until this is the only ground for rejection of either claims 1, 10, 14, and 25 of the instant application or claims 7, 8, 16, 17, and 29 of a co-pending application No. 10/962,732.

PROVISIONAL OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION (NEW)

The Examiner further rejected claims 1, 10, 14, 24, 25, 85-87 and 89 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-17, and 29 of a co-pending application No. 10/962,732.

MPEP § 804(I)(B)(1) recites as follows:

> [i]f a 'provisional' nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in

> the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicant respectfully notes that the instant application was filed on November 25, 2003 while application No. 10/962,732 was filed later, on October 12, 2004. Therefore, the instant application is the earlier-filed application of the two applications. Applicant further notes that as of May 21, 2007, no action on merits have been taken regarding the later-filed application No. 10/962,732.

Accordingly, without making any admissions or agreeing with the Examiner, Applicant respectfully requests postponement of any action on this ground of rejection until this is the only ground for rejection of either claims 1, 10, 14, and 25 of the instant application or claims 1- 17, and 29 of a co-pending application No. 10/962,732

REJECTION ON THE BASIS OF 35 U.S.C. §103

The Examiner has rejected claims 1, 10, 14, 24, 25, 86, 87 and 89 under 35 U.S.C. § 103 as being allegedly unpatentable over Xia et al. (2002) *Nature* 20:1006-1010; Driscoll et al. (WO 01/49844); Cahill et al. (1995) *Atlas of Human Cross-sectional Anatomy,* Wiley-Liss, 3rd ed.; Serra et al. (1996) *Medical Image Analysis* 1(4):317-329; Morel et al. (1997) *J. Comparative Neurology* 387-:588-630; Clark et al. (1997) *J. Neuroscience* 17:7385-7395; Salehi et al. (1999) *J. Neural Transm.* 106:955-986; Whitesell et al. (1993) *Proc. Natl. Acad. Sci.* 90:4665-4669; Davidson et al. (US Patent Application Publication 2004/0023390); Matilla et al. (1998) *J. Neuroscience* 18:5508-5516; Exhibit A: NCBI published mRNA sequence of SCA1 (Mar. 24, 1999) and Caplen et al. (2002) *Human Molecular Genetics* 11: 175-184.

Applicant thanks the Examiner for allowing claim 88 as well as agreeing to a personal interview to better describe the instant invention. During the interview, the Applicant Dr. W. Kaemmerer, explained the meaning of the term "mapping means" and provided evidence that mapping means described in the references used by the Examiners are unsuitable for the instant invention, i.e., delivering siRNA into a predetermined location of a human patient. Even though simple stereotactic surgery described in the references brought forth by the Examiner may be suitable for locating targets in rodent

brains, these means are extremely imprecise and therefore unsuitable for therapy of a relatively large subject (e.g., a sheep or a human). In fact, the mapping means which are necessary for locating a predetermined location in a brain of a human patient are patient-specific and preferably image guided. Applicant respectfully notes that during the interview the Examiner stated that in Office Actions for applications drawn to siRNA therapy, USPTO Examining Unit 1635 routinely cites McCaffrey et al which states that the delivery of siRNA to a target location within a patient has been a problem. The Applicant solved this problem by providing a system which allows for a precise delivery of the siRNA into the targeted location within a patient.

It was agreed that the Applicant will add the limitation of claim 88 (siRNA of SEQ. ID. NO.: 1 or 2) into claim 1. It was further agreed that the limitation requiring that the siRNA bind the target mRNA at least 9 bp downstream of the transcription start site should be removed. Accordingly, claim 1 has been amended to incorporate the limitations of claim 88. Since claim 88 is allowable, claim 1, which incorporates all elements of claim 88 is also allowable. Claims 10, 14, 24, 25, 86, 87 and 89 depend on claim 1, thus incorporating all limitations of claim 1. Since claim 1 is allowable, claims 10, 14, 24, 25, 86, 87 and 89 are also allowable. Accordingly, Applicant respectfully requests the Examiner to withdrawn this ground for rejection.

Applicant respectfully submits that the pending claims are valid and favorable reconsideration and allowance are earnestly solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that the Examiner telephone Applicant's attorney at (609) 844-3020 to discuss any additional rejections.

The USPTO is authorized to charge Deposit Account No. 50-1943 for any charges in connection with this matter.

Respectfully submitted,

Date: June 5, 2007

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ATTACHMENT 1